ABNORMAL EMOTIONAL STATES IN RELATION TO

THE PANCREAS.

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ABNORMAL EMOTIONAL STATES IN RELATION TO THE PANCREAS.

In an investigation of the surface tension variations in the sera of the blood of a large number of patients suffering from a variety of mental disorders, carried out at Bethlem Royal Hospital[1] it was found that these variations were most marked in cases exhibiting abnormal emotion.

The normal variation in the surface tension of the blood serum is from 41.5 dynes per c.m. unheated to 46 dynes per c.m., when heated to 56°C. for half an hour.[2]

Practically all the cases where emotion was or had been excessive, showed an abnormally low range of surface tension. Experimenting with numerous substances in an endeavour to increase the range of surface tension in these cases, Lovell (op. cit.) at length used "Secretogen", a pancreatic stimulant of the same nature as secretin.

This was used as the result of a case of Agitated Melancholia which post-mortem showed an extensive destruction

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(1) Clement Lovell, M.D., Journal of Mental Science, October 1923, p.497.

(2) Clement Lovell, M.D., Journal of Neurology and Psychopathology, August 1922.

of the pancreas, a condition which had not been suspected during life. Also Downs and Eddy[1] had shown that Secretin produced blood changes in rabbits when given subcutaneously. Lovell (op. cit.) found that Secretogen was very effective in bringing the range of surface tension back to normal, and, coincidentally with this, the patients improved.

The results were so striking that the question was raised as to whether the abnormal emotional state might be primarily due to a pancreatic lesion leading to an interference with the endocrine balance.

All pancreases of patients dying from various mental disorders were then examined, and a majority of agitated melancholias showed changes in the interlobular tissue, varying from an increased nucleation of the connective tissue, in patches, to widespread acute pancreatitis, and even to fibrosis

Autolytic changes in the pancreas are so variable that no conclusions can be drawn from the appearance of the parenchyma alone.

But as these patients had all died from some intercurrent disease, infiltration of the pancreas was not sufficient proof of the causal relationship between the pancreas and the emotional state.

It was therefore necessary to apply collateral tests.

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(1) Downs and Eddy, American Journal of Physiology, December 1921.

The accompanying photographs show changes in the pancreas in cases dying from various disorders.

PLATE I. Patient died of Miliary Tuberculosis. Pancreas normal.

PLATE II. For three months prior to death from Pneumonia patient was depressed and hyper-emotional, and suffered from apprehension of torture. Pancreas shows early infiltration of the interlobular tissue.

PLATE III. Patient died of Uraemia. Was depressed and hallucinated. It was not known for how long a time this condition had existed. Pancreas shows very much increased nucleation of connective tissue.

PLATE IV. A case of Agitated Melancholia of five months' duration. Patient died of Pancreatitis with haemorrhage.
Pancreas shows thrombosis and haemorrhage.

PLATE V. Agitated Melancholia. Duration two years. Died of Pulmonary Tuberculosis. Pancreatitis and considerable fibrosis of the interlobular tissue.

PLATE VI. Agitated Melancholia. Duration about six months. Death from Bronchitis.
Pancreas shows considerable interlobular fibrosis and much increased nucleation.

PLATE VII. Agitated Melancholia. Duration seven months. Death from Pulmonary Tuberculosis.
Pancreas shows extensive interlobular fibrosis.

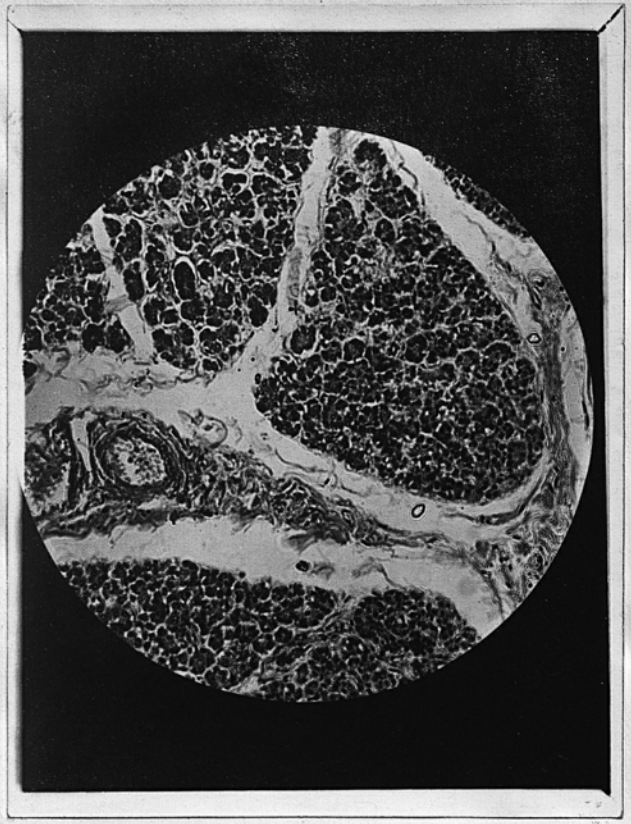

PLATE I.

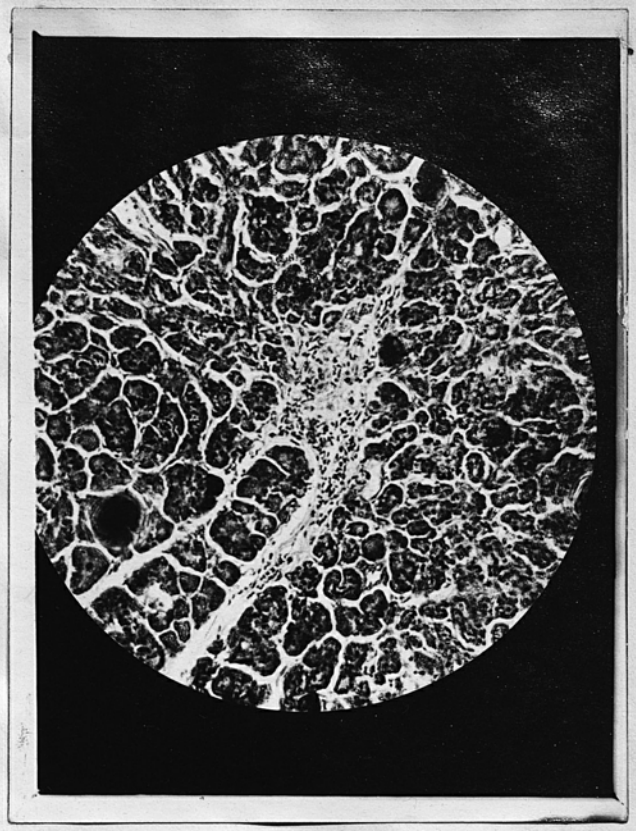

PLATE II.

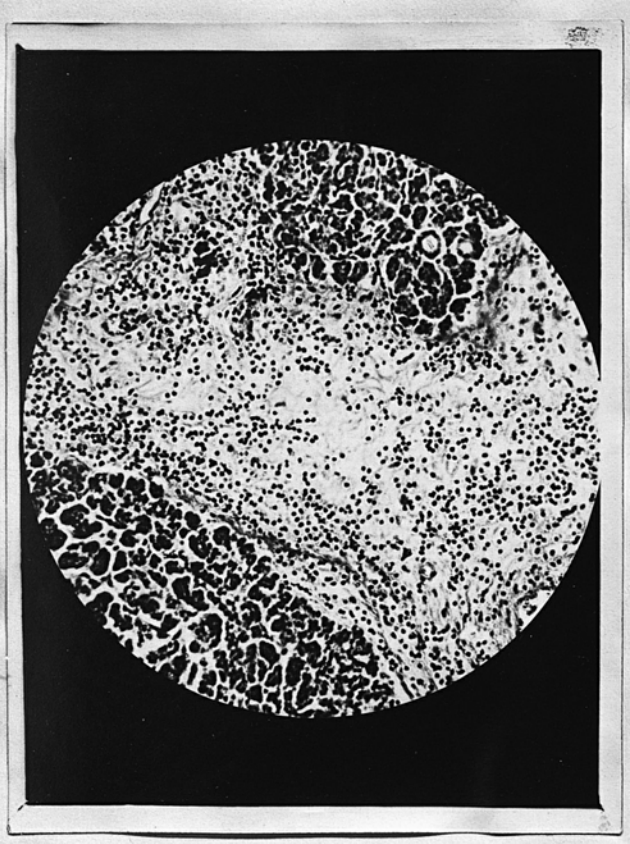

PLATE III.

PLATE IV.

PLATE V.

PLATE VI.

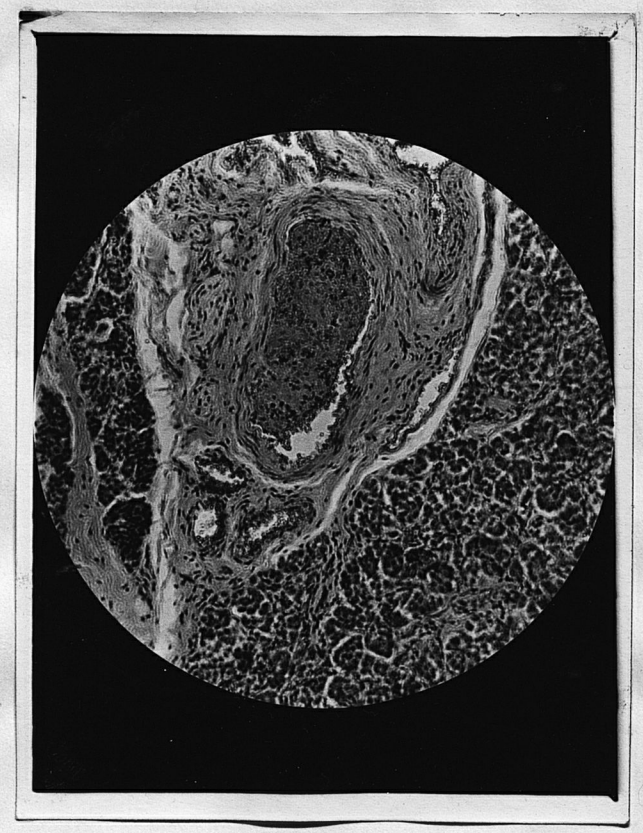

PLATE VII.

There was little opportunity of examining the pancreases of other cases of abnormal emotional states, such as Anxiety Neurosis or Obsessional Neurosis, as these cases do not usually die while under observation.

It then became desirable to apply the accepted tests for pancreatic efficiency to a number of cases of different clinical diagnosis, but having as a common factor an abnormal emotional state.

No one functional test is pathognomonic of disease of the pancreas on account of the several different functions of the organ.

The diastase test was used at first but was later discarded, because it was complicated by the question of renal insufficiency.

Two tests were eventually chosen.

The first, the Sajodin or Monoidobehenate of Calcium test, suggested by Winternitz, is a test of the fat digestive power of the pancreas and is thus a test of its external secretory capacity.

The second was Loewi's adrenalin pupil reaction test. This concerns the internal secretory function of the pancreas.

Sajodin contains 25% of iodine in combination with fats. In a normal person if 3 grammes of Sajodin are given by the mouth with a meal, iodine can be found in the urine within

four hours, having been liberated by the fat splitting ferment, Steapsin. This does not occur in a fasting person, as no flow of pancreatic juice has been stimulated.

Also in the case of jaundice the absence of bile salts in the intestines would prevent the action of Steapsin on the Sajodin.

Delay or complete absence of iodine in the urine in from four to six hours after ingestion with a meal, is taken to mean lypolytic pancreatic insufficiency.

There is an important fallacy, however.

Delayed appearance of iodine in the urine may be due to intestinal stasis, an exceedingly common condition in melancholia and many other mental disorders.

To rule out this fallacy it was necessary to work out the ratio of ethereal to inorganic sulphates in the cases tested.

The value of this test is corroborated by Stegman[1] and also by Syring.[2]

In the case of the second test, Loewi considers that the internal secretion of the pancreas, besides controlling the carbohydrate metabolism of the body, exercises an inhibitory effect upon the sympathetic.

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(1) Ueber eine neue Methode der Pankreasfunctionsprüfung Winternitz Diagnostikum. Dissertazione Otto Stegman, 1911.

(2) Ueber die Funktionsprüfung des Pankreas. Syring, Leipzig, 1913.

In 1908[1] he found that after the extirpation of the pancreas in certain animals, instillation of adrenalin into the eye caused a dilatation of the pupil. Normally this does not occur.

Loewi put forward the supposition that in man mydriasis following instillation of adrenalin into the eye would indicate pancreatic insufficiency of the internal secretion so long as over-action of the thyroid or suprarenal can be excluded.

It may be noted that the pancreatic deficiency may be absolute, or it may be relative to a hyper-activity of the thyroid or suprarenal.

Sladden[2] lays emphasis on the value of this test.

Also the positive results found in the pancreatic insufficiency of diabetes are corroborated by Falta[3] and also by Zak[4].

In the performance of the test, an ophthalmic disc of adrenalin gr. $\frac{1}{200}$ was placed upon the conjunctiva.

Where the test was positive, dilatation and often irreg-

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(1) Archives of Experimental Path. and Pharm. 1908 LIX 83.

(2) Sladden - Quarterly Journal of Medicine, 1913-14, VII.455.

(3) Falta. Wien. Klein. Wohnschr. 20, 1907. 1559.

(4) Zak. Verhand. d. 25 Kong. f. inner Med. 1908, 392.

ularity took place within about half an hour.

The Sajodin test was performed in a series of 80 cases of a variety of mental disorders, taken at random; most of which showed an abnormal emotional state.

Three grammes of Sajodin in powder form were mixed up with the food at the midday meal, and samples of urine were taken at intervals of 4 hours and 6 hours after the meal.

To a sample of urine a few drops of 2% Sodium Nitrite solution and a few drops of 10% Sulphuric Acid were added in order to set free the iodine; then 1 c.c. of Starch Solution. Blue colouration indicated the presence of iodine.

Of the 80 cases examined, 60 either exhibited or had exhibited, as far as could be ascertained, abnormal emotion - i.e. 75%. Of these 80 cases 23 gave an abnormal reaction to the Sajodin test, i.e. 28.7%.

After several weeks these tests were carried out again. The results were found to remain consistently the same. The urine of these cases giving an abnormal Sajodin reaction was examined for the ratio of ethereal sulphates to inorganic sulphates, in order to rule out the possibility of an abnormal result being due to intestinal stasis.

Of these 23 cases, 6 gave an anbormal ratio, i.e., less than 1.7%. These cases were ruled out.

Dr. Lovell examined the surface tension of the serum in each of these 23 cases. Fourteen gave an abnormal range,

taking as abnormal any range below $3\frac{1}{2}$ dynes.

Two of these cases, however, had given an abnormal sulphate ratio and must be discarded.

Of the 17 cases giving the positive Sajodin test (having omitted the six with an abnormal sulphate ratio), twelve gave an abnormal range of surface tension, i.e. 70.5%, and in each of these cases abnormal emotion or anxiety was or had been a prominent feature.

Of the 17 cases, 10 also gave a positive result to the Loewi test, i.e. 58.8%.

Six out of the 80 cases showed abnormal emotion, gave an abnormally low range of surface tension, a positive result to the Sajodin test and to the Loewi test, i.e. 7.5%.

	Name	Disease	Abnormal Emotion	Sajodin Test	Sulphate Ratio	Surface Tension	Loewi Test
1.	M.L.	Chronic Alcoholism	-	-			
2.	A.M.	Neurasthenia	-	-			
3.	J.S.	Neurasthenia	-	-			
4.	F.C.	Simple Melancholia	+	+	1:8	41.5-46	-
5.	A.F.A.	Obsessional Neurosis	+	-			
6.	D.R.	Paraphrenia	+	+	1:8	41.5-46	+
7.	F.W.	High-grade Defective	-	-			
8.	F.S.	Simple Melancholia	+	+	1:5	40-44.5	+
9.	S.B.	Adolescent Instability	-	+	1:6	38-43	-
10.	F.P.	Recurrent Mania	+	+	1:4	39-42.5	-
11.	H.R.E.	Dementia Praecox	+	+	1:7	44-40.5	-
12.	H.B.	Acute Confusional Insan	+	-			
13.	R.G.	Adolescent Instability	-	-			
14.	J.H.	Chronic Melancholia	+	-			
15.	J.P.	Chronic Melancholia	+	-			

Name	Disease	Abnormal Emotion	Sajodin Test	Sulphate Ratio	Surface Tension	Loewi Test
16. S.F.	Neurasthenia	+	-			
17. G.L.	Senility	-	-			
18. C.D.	Manic-Depressive-Insan.	+	-			
19. G.M.	Acute Confusional Insan.	+	-			
20. S.D.	Dementia Praecox	-	-			
21. G.M.	Senility	+	-			
22. A.C.	Neurasthenia	-	-			
23. H.A.K.A.	General Paralysis	-	-			
24. P.G.G.	Paranoia	+	+	1:10	41.5-45	+
25. F.S.	Chronic Melancholia	+	+	1:4	38-44	-
26. K.L.	Chronic Melancholia	+	-			
27. F.H.E.	Agitated Melancholia	+	+	1:10	41-41.5	+
28. S.J.	Neurasthenia	-	-			
29. T.R.	Agitated Melancholia	+	-			
30. C.L.	Chronic Melancholia	+	-			
31. C.S.	Chronic Melancholia	+	-			
32. S.M.	Neurasthenia	+	-			
33. A.S.J.	Neurasthenia	+	+	1:12	43-45	-
34. W.T.R.	Paranoia	-	-			
35. C.P.	Agitated Melancholia	+	+	1:6	42-39	+
36. E.D.H.B.	Senility	+	-			
37. J.L.	Chronic Melancholia	+	-			
38. R.C.C.	Dementia Praecox	-	-			
39. E.L.P.	Simple Melancholia	+	-			
40. R.N.	Chronic Melancholia	+	-			
41. D.C.H.	Recurrent Mania	+	-			
42. M.P.	Chronic Mania	+	-			
43. L.R.C.	Neurasthenia	-	-			
44. S.F.V.	Chronic Mania	+	+	1:7	42-44.5	+
45. G.H.J.	Acute Confusional Insan.	+	-			
46. H.B.	Chronic Melancholia	+	-			
47. J. McC.	Simple Melancholia	+	-			
48. H.S.	Chronic Melancholia	+	+	1:13	44.5-40.5	+
49. F.A.G.	Anxiety Neurosis	+	+	1:11	45-47	-
50. L.P.	Chronic Melancholia	+	-			
51. S.A.H.	Neurasthenia	-	-			
52. B.E.H.	Chronic Melancholia	+	+	1:7	43.5-41.5	-
53. F.H.B.	Obsessional Neurosis	+	-			
54. S.R.S.	Anxiety Neurosis	+	+	1:7	39-45	+
55. E.B.	Neurasthenia	-	-			
56. E.W.	Paraphrenia	+	-			
57. L.C.H.	Dementia Praecox	-	-			
58. A.D.R.	Recurrent Mania	+	-			
59. C.G.R.	Acute Confusional Insan	+	-			
60. S.H.	Paranoia	+	-			

Name	Disease	Abnormal Emotion.	Sajodin Test	Sulphate Ratio	Surface Tension	Loewi Test
61. E.R.D.M.	Acute Confusional Insan.	+	-			
62. R.T.H.	Agitated Melancholia	+	-			
63. N.K.J.	Acute Confusional Insan,	+	-			
64. A.G.R.	Puerperal Insanity	+	+	1:7	40.5-38.5	+
65. E.S.M.	Agitated Melancholia	+	-			
66. H.D.S.	Paraphrenia	+	-			
67. A.G.W.	Hysteria	+	-			
68. H.B.	Paranoia	-	-			
69. E.G.H.	Simple Melancholia	+	+	1:12	38.5-44.3	+
70. W.D.P.	Chronic Melancholia	+	+	1:6	41 - 43	-
71. D.M.G.	Simple Melancholia	+	-			
72. M.E.K.	Obsessional Neurosis	+	-			
73. G.B.	Puerperal Insanity	+	+	1:8	45-44.5	-
74. P.G.	Chronic Melancholia	+	+	1:10	42.5-43	+
75, G.S.B.	Neurasthenia	-	-			
76. F.M.	Simple Melancholia	+	-			
77. S.W.	Paraphrenia	-	-			
78. L.R.N.	Neurasthenia	+	-			
79. E.M.S.	Neurasthenia	+	+	1:11	41.5-40	-
80. N.W.	Agitated Melancholia	+	+	1:11	40-40	+

	Number	Abnormal Emotion	+ Sajodin.	Abnormal S.T.	Abnormal Sulph. Ratio	Abnormal Loewi
Manic.Depress. Insan.	1	1				
Simple Melancholia	7	7	3		1	2
Chronic Melancholia	14	14	5	4	2	2
Agitated Melancholia	6	6	3	3	1	3
Rec. or Chr. Mania	5	5	2	1	1	1
Paranoia	4	2	1			1
Paraphrenia	4	3	1			1
Dementia Praecox	4	1	1	1		
Amentia - High Grade	1					
Adolescent Instability	2		1		1	
Acute Conf. Insanity	6	6				
Puerperal Insanity	2	2	2	2		1
Alcoholism	1					
Anxiety Neurosis	2	2	2	1		1
Obsessional Neurosis	3	3				
Neurasthenia	13	5	2	2		
Hysteria	1	1				
Senility	3	2				
General Paralysis	1					
	80	60	23	14	6	12

The 12 cases showing abnormal emotion and giving a lowered range of surface tension of the serum and a positive Sajodin test were as follows:-

Chronic Melancholia	...	3
Agitated Melancholia	...	2
Chronic Mania	...	1
Dementia Praecox	...	1
Puerperal Insanity	...	2
Anxiety Neurosis	...	1
Neurasthenia	...	2

Of these the following also gave a positive reaction to the Loewi Test:-

Chronic Melancholia	...	2
Agitated Melancholia	...	2
Chronic Mania	...	1
Puerperal Insanity	...	1

None of these cases gave any clinical indication of hyper-thyroidism.

These results seem to show that there is a very definite relation between a certain group of cases manifesting abnormal emotional symptoms and disturbances of the pancreas.

The cases are not definitely confined to any one clinical group.

Post mortem it can be verified microscopically in a certain number of chronic melancholias and agitated melancholias. During life, so far as the pancreatic tests are indicative of pancreatic defect, some of these same clinical types and also a certain number of the more acute anxiety disorders, such as the Anxiety Neurosis and Obsessional Neurosis, suggest a

primary pancreatic disturbance. The exact mechanism which connects pancreatic deficiency with an abnormal surface tension, and emotional and anxiety states, is not yet clear.

Some undoubted cases of pancreatic disease show no anxiety symptoms.

As to the cause of the pancreatic lesion, organisms can sometimes be found which are agglutinated by the patient's serum. This may possibly be responsible for the infiltration of the pancreas.

A small proportion of cases agglutinate their own B. Proteus, and infection of the pancreas by B. Proteus has long been recognised.

The pancreases of some Chronic Melancholias are quite fibrosed, probably as a result of prolonged inflammation of low virulence, in contradistinction to those of Agitated Melancholia where the inflammatory processes are more acute.

Many of these patients have developed their disease after an attack of Influenza or infections of the alimentary tract.

Some of them also have gall-stones, from a concomitant infection of the liver ducts.

Often there is a history of sudden onset with acute abdominal pain. In the treatment of these cases, if an organism can be isolated which is agglutinated by the patient's serum a vaccine may be helpful.

The infiltratuon of the pancreas is patchy in its distribu-

tion, so that vaccine treatment is not without danger of causing an obstruction of the pancreatic ducts which might lead to necrosis.

A certain number have been treated by the sour milk treatment. It is a matter of clinical experience that Lactic Acid alone produces no improvement, but the Lactic Acid with the milk fat is more active.(1)

Secretogen if given to the right case is extremely effective in increasing the range of surface tension.

It is usually possible to bring the range back to normal within about 10 days by giving 2dr. twice daily, and it has been repeatedly found that the condition of the patient improves pari passu with the range of surface tension.

SUMMARY.

1. The Sajodin test is only of value if taken in conjunction with such other factors as intestinal stasis.
2. The results of the Loewi Test appear to indicate that one can have a pancreatic insufficiency which is either absolute, or simply relative to suprarenal or thyroid excess.
3. All the cases which gave a positive result to all the pancreatic tests, showed or had shown abnormal emotional states.
4. All patients with abnormal emotional states do not show

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(1) J.G. Porter Phillips - Journal of Mental Science, July 1910.

pancreatic insufficiency by these tests.

5. Therefore there appears to be a group of patients whose mental state is intimately associated with abnormality of the pancreas but as is to be expected this pathological group does not correspond with any clinical group.

My thanks are due to the Governors of Bethlem Royal Hospital and to the Superintendent, Dr. J.G. Porter Phillips, for the opportunity of carrying out this work.
